
OFFICE OF NEW ANIMAL DRUG EVALUATION
REVIEWERS' CHAPTER

APPROVAL PROCESS AND APPROVAL PACKAGE

I. PURPOSE OF GUIDE

This Guide describes the procedures for preparing and routing original NADA packages.

The same general procedures that apply to preparing and routing of a package for approval of an original New Animal Drug Application (NADA) apply to Abbreviated New Animal Drug Applications (ANADAs) and supplemental NADAs requiring a Federal Register (FR) publication.

II. PROCEDURE

The primary division reviewer prepares a variety of documents as part of an approval package (i.e., Memorandum Recommending Approval (MRA), Freedom of Information (FOI) Summary and Approval Letter). The reviewer also provides information to HFV-6, Policy and Regulations Team, to support a request for preparation of a draft FR notice (draft regulation). The information needed to

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initiate the process is described in Center for Veterinary Medicine (CVM) Policy and Procedures Guide (CVM P&P Guide) 1240.3125, Preparation of a Draft Federal Register Notice of Approval of a New Animal Drug Application. The procedures for NADAs and ANADAs are the same except where indicated.

III. NADA/ANADA APPROVAL PACKAGE

This section describes the general procedures for preparing an approval package for an original NADA. The same procedures apply to preparing approval packages for a supplemental NADA or ANADA.

Contents of an approval package:
An approval package consists of two folders (A & B) containing reviews and summary documents and the original NADA or ANADA jackets containing the pending submission(s).

Folder A (details follow later in this section):
This folder (pocket folders are preferred) contains one draft copy (so changes can be made) of each of the following:

- Draft regulation
- Draft Memorandum Recommending Approval (MRA)
- Draft FOI Summary (plus *Signature Page* – see **Attachment** for example of Signature Page for the FOI Summary)
- Draft Approval Letter
- Environmental document (e.g., FONSI and EA), if required.
- Facsimile or final printed labeling (attached to the back of the FOI Summary)

Folder B (details follow later in this section):
This folder (pocket folders are preferred) contains scientific reviews and other pertinent information (e.g., BIMO, DER, GMP status, etc.) that support the approval. Folder B documents are in final with appropriate copies included and marked for distribution.

DETAILS OF FOLDER A CONTENTS

A. Draft Regulation:

- The draft regulation is included in Folder A. Making copies of the draft regulation for specialty units is discouraged because revisions in the document are made prior to publication, and a file copy would not necessarily be a true copy. Only the actual Federal Register publication should be used to make such file copies.

- Each person reviewing the package signs the blue cover page of the draft regulation to indicate concurrence with the action. The Mail Code and date of signature accompany the signature.

- Any revision, change, or correction made on the draft regulation must be initialed and dated when made.

B. Memorandum Recommending Approval (MRA):

The purposes of the MRA follow:

(1) To provide a brief overview of the basis of our recommendation for approval to the signature authority;
(2) To reference the component documents which support approval (who reviewed what and when; final conclusions);
(3) To provide a checklist for consistency of basis of approval across the animal drug industry;
(4) To transmit a formal recommendation from the Reviewer/Team/ Division to the approval authority.

- The Reviewer, Team Leader, and Division Director sign the MRA. For Original approvals, the MRA is addressed to the Center Director through the Director, ONADE. Supplemental approvals involving a new claim, new species, or a change in RX/OTC status are also addressed to the Center Director. All other supplemental approvals are addressed to the Director, ONADE, except certain Chemistry supplements that are handled by the Division of

Manufacturing Technologies (HFV-140) and are signed by the Director, Division of Manufacturing Technologies.

- Distribution of MRA:
  See CVM P&P Guides 1243.5740, ANADA MRA or 1243.5741, NADA MRA.

NOTES:
Only one copy of the draft MRA is sent forward initially with the Approval Package. Once all the reviewing officials (See CVM P&P Guides 1243.5740, ANADA MRA or 1243.5741, NADA MRA) concur, corrections are made to the draft, and then the final copies for distribution are made.

The final original copy (on white paper) is filed in the application jacket. No salmon copy is needed.

- The GMP status for original applications and supplements is ascertained and reported in the MRA prior to forwarding the approval package. Refer to CVM P&P Guides 1243.5740, ANADA MRA; 1243.5741, NADA MRA; and 1240.3200, Routing a Request for Review.

C. FOI Summary:

The Freedom of Information (FOI) Summary is included in Folder A.

- The initial decision package contains a single draft copy of the FOI Summary with an accompanying signature page. Once all reviewing officials have concurred with the FOI and the designated changes have been made, the final printed copies are made and marked for distribution. All copies are then placed in Folder A and forwarded to Team Leader, Division Director, HFV-150 (if necessary), HFV-102, HFV-100 and HFV-1 (for original applications and supplemental applications which cover new species, new claims, and a shift from Rx to OTC status) for signature. For further information, see CVM P&P Guide 1243.3060, Final Document Routing and Copy Distribution for

NADAs, ANADAs, INADs, Master Files, and Suitability Petitions for a complete description.

- HFV-102 will stamp date the FOI Summary copies with the same date the Approval Letter issues, and will fax a courtesy copy of the Approval Letter to the sponsor. HFV-103, Document Control Unit, issues all letters and enters final action codes in STARS.

- For the distribution copies for the FOI Summary, refer to CVM P&P Guides 1243.5760, FOI Summary for an ANADA; 2143.5761, FOI Summary for an NADA; and 1243.5762, FOI Summary for a Combination Drug Approval. A copy of the labeling accompanies each copy of the FOI Summary.

D. Approval Letter:

Steps in processing the Approval Letter follow:

- Following concurrence by all reviewing officials on the draft Approval Letter, the primary division reviewer may decide to document the date and the official who reviewed and signed the draft package. Some reviewers find it useful to use a table that includes officials mail code, name, and date they signed. The table should follow the *cc: block*. See the table below. Then, the final copies are printed and marked for distribution.

Office	Surname	Date Draft Signed	Date Final Signed
Team HFV #			
DD HFV #			
QA Team HFV 102			

An addressed envelope of appropriate size is also included. [A large manila envelope is required if a copy of the FOI is being transmitted to the sponsor].

- Each person concurring with the approval action initials the HFV-199 (salmon) copy, and includes the mail code and date of signature. This may be done in the table if one is created by the reviewer.

- Original. The original Approval Letter (on letterhead bond) is signed by HFV-100 or HFV-1 (as determined by signature authority), stamp dated, and mailed to the drug sponsor. HFV-1 signs all Approval Letters for original NADAs/ANADAs, and major supplements (new species, new indications, Rx to OTC status). HFV-100 signs all other approvals except for the manufacturing chemistry supplements.

- Distribution copies for the Approval Letter (original and all copies are date-stamped by HFV-102: HFV-102 faxes a courtesy copy of the Approval Letter to the sponsor with no *cc: block*). Refer to CVM P&P Guide 1243.3060, Final Document Routing and Copy Distribution for NADAs, ANADAs, INADs, Master Files, and Suitability Petitions.

NOTES:
Only one copy of the Approval Letter is sent forward initially with the Approval Package. After the reviewing officials concur and necessary corrections are made to the draft Approval Letter, then copies for distribution are included.

A copy should be provided to the FDA DO for a sponsor's headquarters and for any FDA DOs identified in the HFV-140 Technical Section Complete letter or Manufacturing Chemistry Review Memoranda (as indicated in the *cc: block*). Guidance on FDA DOs is provided in P&P Guide 1243.3300, Copies of Correspondence to FDA District Offices (go to link below):
www.fda.gov/cvm/index/policy_proced/ppindex.html

E. Environmental Assessments, Finding of No Significant Impact, and Environmental Impact Statements:

- If the action is not categorically excluded, the decision package contains a final Finding of No Significant Impact (FONSI) and Environmental Assessment (EA) or an Environmental Impact Statement (EIS) and record of

decision. The signed original is included in Folder A and sent to HFA-305, Dockets Management Branch.

- Only one copy of the environmental document, e.g., FONSI, EA, or EIS is sent to HFV-102 initially in Folder A with the Approval Package.

- Environmental Documents, distribution copies:

  cc:

  HFV-199, NADA Orig., filed by DCU

  HFV-102, Reserve Copy

  HFV-145, Environmental Assessment Team

  HFV-*xxx*, (any other copies are optional)

F. Facsimile or Final Printed Labeling:

A copy of the final printed labeling or the facsimile labeling, as provided by the sponsor, should be included in Folder A. It is attached to the back of the FOI Summary.

DETAILS OF FOLDER B CONTENTS

Reviews and other Pertinent Documents:

- Folder B of the approval package contains all specialty reviews and any routine administrative memos. It also may contain a Document Summary or a Veterinary Medical Review, if required.

- Copies of all pertinent documents are required for the original NADA (HFV-199) and the Team or Division file. Any other copies are optional.

IV. PROCEDURES FOR ROUTING AND DISTRIBUTION OF APPROVAL PACKAGE

A. The approval will be routed from the target animal review team to the following stops via a STARS Tracking Form for Approvals Requiring Administrative Review (printed on yellow paper): Team Leader, Division Director, HFV-103, HFV-150 (if needed), HFV-103, HFV-102, GCF-1 (if needed), HFV-100, HFV-1 (if appropriate), HFV-102, HFV-103, and HFV-199. Each time the document moves, it is logged through HFV-103 for STARS tracking. The DCU assures that the header information is correct for the STARS database, and assures proper filing of the Federal Register document, FOI Summary, labeling, Approval Letter, MRA, and other documents into the NADA file.

B. The actual routing of an approval package with a draft regulation (through the draft approval and final approval process) is as follows:

NOTE: The Administrative NADA working group has completed a flow chart of the approval process with annotations. It can be found on the S: drive of the network.

- The primary division reviewer prepares Folders A and B (see Folder A and B Contents box). An NADA Day is scheduled, if necessary. The reviewer should check with their Team Leader to determine if an NADA Day or any other special administrative steps are needed.

- The reviewer determines if the approval will result in a change to the regulations. Most approvals require preparation of a draft Federal Register document announcing approval of a New Animal Drug Application ("draft regulation"). Exceptions include most manufacturing supplements and some labeling changes.

- If the approval will require a change or addition to the regulations, the reviewer sends a request to the Policy and Regulations Team (HFV-6) to prepare a draft regulation. If the approval does not require a draft regulation from HFV-6, it goes directly from the reviewer to the Team Leader.

HFV-6 prepares the draft Federal Register document, assigns a Federal Register Document Tracking System (FRDTS) number, and works with the primary division reviewer to make sure the draft regulation is accurate. Upon completion, HFV-6 forwards the draft regulation to the target animal division reviewer through the DCU.

The primary division reviewer checks the draft Federal Register document to make sure the information is accurate and complete.

The reviewer adds the draft Federal Register document to Folder A and sends the entire approval package (Folders A & B and the volume of the sponsor's submission with the STARS Routing Slip) to their Team Leader. The Team Leader reviews/edits the package, signs off on it, and sends it to the Division Director.

- The Division Director reviews/edits the approval package and signs off on it.

  If the approval package contains an EA and FONSI or EIS, then the Team Leader of the Environmental Assessment Team (HFV-145) reviews the approval package; otherwise, the approval package is sent forward.

  HFV-145 reviews the EA and FONSI or EIS for accuracy and completeness. Then the package is sent to forward to HFV-150 or the Quality Assurance Team (HFV-102).

- If the approval is for use in food-producing animals, the Division of Human Food Safety (HFV-150) reviews the approval package; otherwise, the approval package is forwarded to the Quality Assurance Team (HFV-102).

  After HFV-150 reviews the human food safety (HFS) section of the approval package for accuracy and completeness, the package is sent to HFV-102.

- The Quality Assurance Team (HFV-102) reviews the entire package for accuracy and completeness (i.e., FOI, MRA, Draft Regulation, labeling, etc.).

  NOTE: If the approval is not for use in food animals, the package goes from the Division Director to HFV-102.

HFV-102 determines whether the Office of Chief Counsel (OCC) should review the draft approval package (See CVM P & P Guide 1240.2020). If OCC review is necessary, the package is forwarded to them for review; otherwise, it is returned to the primary division through DCU.

- If OCC review is required, OCC reviews the draft approval package for compliance with the Act, implementing regulations, and Agency policies. OCC returns the package to HFV-102. Then HFV-102 returns the draft approval package with comments to the target animal division via the DCU.

Once the reviewer has taken the draft approval package and put it into final format, the final approval package is routed in the following manner:

- The Team Leader reviews the package. If errors are found, it is returned to the reviewer so that the errors can be corrected. The Team Leader signs off on the final approval package.

- The Division Director reviews the package. If errors are found, it is returned to the Team (Team Leader or reviewer) so that the errors can be corrected. The Division Director signs off on the final approval package.

- If any changes have been made to the human food safety information since the draft approval process, or if changes were requested during the draft approval process, or if the approval will result in a change to the human food safety regulation (21 CFR 556), then the final approval package must be sent to HFV-150 for concurrence.

  Also, If any changes have been made to the EA, FONSI or EIS, then the final approval package must be sent to HFV-145 for concurrence.

  If not, the final approval package goes to HFV-102 through DCU.

  HFV-150 reviews the final approval package. If errors are found, the package is returned to the primary review division so that the errors can be corrected. HFV-150 signs off on the final approval package and routes it to HFV-102 through the DCU.

- HFV-102 reviews the final approval package. If errors are found, the package is returned to the primary review division so that the errors can be corrected. HFV-102 signs off on the final approval package. The package is then sent through the DCU to the Office Director.

- The Office Director (HFV-100) reviews the final approval package. If errors are found, the package is returned to the primary review division so that the errors can be corrected. HFV-100 signs off on the final approval package.

- If the application involves an original approval or a supplemental approval for a new species, a new indication, and/or the change in status of a prescription drug (Rx) to an over-the-counter drug (OTC), the approval package is sent to the Center Director (HFV-1) for signature.

  If not, the package goes from HFV-100 to HFV-102.

- HFV-1 reviews the final approval package. If errors are found, the package is returned to the target animal review division so that the errors can be corrected. HFV-1 signs off on the final approval package. HFV-1 forwards the signed package to HFV-102.

- HFV-102 processes the final approval package. (See Codification and Public Display Section below.)

- The final package is returned to the document control unit (in this case, the code on the transmittal sheet is HFV-199) and is filed, and approval documents are distributed.

Routing for the Codification and Public Display of an Approval:

- HFV-102 sends the draft Federal Register document to HFV-6 to be put into final.

- The regulation is logged through the FRDTS to the Regulations Editorial Staff (RES, HF-27), which prepares the final Federal Register document (regulation) for publication in the FR.

- The final Federal Register document is sent back through FRDTS and is returned through HFV-6 to obtain appropriate signatures.

- HFV-102 consolidates the following documents to be forwarded with the final Federal Register document: FOI Summary with attached labeling, appropriate environmental documents (EA and FONSI or EIS), and any regulatory analytical methods for residue.

- If the application involves an original approval or a supplemental approval for a new species, a new indication, and/or the change in status of a prescription drug (Rx) to an over-the-counter drug (OTC), the final Federal Register document is sent to the Center Director (HFV-1) for signature. Final Federal Register documents relating to other approvals except manufacturing supplements are sent to the Director of ONADE (HFV-100) for signature.

  The Director of the Division of Manufacturing Technologies signs for manufacturing supplements.

- The final Federal Register document goes to HFV-102 and is forwarded to RES for publication.

- The final Federal Register document goes back through FRDTS to RES. RES forwards the following:

  1) The final Federal Register document to the Office of the Federal Register (OFR) for publication in the FR and codification in the Code of Federal Regulations (CFR), and
  2) The public display documents (FOI Summary with attached labeling, appropriate environmental documents, and any regulatory analytical methods for residue) to the Dockets Management Branch (HFA-305).

- The final Federal Register document and the public display documents (FOI Summary with attached labeling, appropriate environmental documents, and any regulatory analytical methods for residue) are placed in the appropriate docket and are available for the public in the Dockets' reading room and on the Dockets' website.

- The final Federal Register document is published in the FR and the approval regulation is codified in the CFR. The Green Book is updated following publication of the approval in the FR.

V. MAIL CODES USED FOR OFFICE IDENTIFICATION IN THIS DOCUMENT

HF-26	Regulations Policy and Management Staff, Division of Regulations Policy, FDA Parklawn, Rm. 12A-17
HF-27	Regulations Editorial Staff, Division of Regulations Policy, FDA Parklawn, Rm. 12A-20
HFV-1	Director, Center for Veterinary Medicine
HFV-6	Policy and Regulations Team, CVM
HFV-10	Office of Management and Communications, CVM
HFV-100	Director, Office of New Animal Drug Evaluation (ONADE)
HFV-101	Generic Drugs Team
HFV-102	Quality Assurance Team
HFV-103	Document Control Unit (STARS Entry; document transfers), CVM
HFV-104	Risk Assesment Team
HFV-105	Biometrics Review Team
HFV-110	Division of Therapeutic Drugs for Non-Food Animals
HFV-120	Division of Production Drugs
HFV-130	Division of Therapeutic Drugs for Food Animals
HFV-140	Division of Manufacturing Technologies
HFV-145	Environmental Assessment Team
HFV-150	Division of Human Food Safety
HFV-199	Document Control Unit, CVM, Final Document Processing and Filing Function
HFV-210	Division of Surveillance, Office of S & C
HFV-216	Post Approval Review Team, Division of Surveillance, Office of S & C
HFV-226	Medicated Feeds Team, Division of Animal Feeds, Office of S & C
HFV-234	Bioresearch Monitoring and Administrative Actions Teams, Division of Compliance, Office of S & C
HFV-*xxx*	A general mail code, indicating any team/staff/division in ONADE
GCF-1	Office of Chief Counsel, Parklawn, Rm. 6-67
HFA-305	Dockets Management Branch, 5630 Fishers Lane, Rm. 1061
HFR-*XXxxx*	A general reference to FDA District Office, indicating the appropriate FDA DO, for example, HFR-MA250, BLT-DO (Refer to CVM P&P Guide 1243.3300, Copies of Correspondence to FDA

	District Offices)

VI. REFERENCES

Section 512 of the Federal Food, Drug, and Cosmetic Act

Code of Federal Regulations, 21 CFR part 5, Delegations of Authority and Organization

CVM Policy and Procedures Manual Guide 1240.3125, Preparation of Draft Federal Register Notice of Approval of a New Animal Drug Application

CVM Policy and Procedures Manual Guide 1243.3300, Copies of Correspondence to FDA District Offices

CVM Policy and Procedures Manual Guide 1243.5740, Abbreviated New Animal Drug Application Memorandum Recommending Approval

CVM Policy and Procedures Manual Guide 1243.5741, New Animal Drug Application Memorandum Recommending Approval

CVM Policy and Procedures Manual Guide 1243.5760, Freedom of Information Summary for an ANADA

CVM Policy and Procedures Manual Guide 1243.5761, Freedom of Information Summary for an NADA

CVM Policy and Procedures Manual Guide 1243.5762, Freedom of Information Summary for a Combination Drug Approval

CVM Policy and Procedures Manual Guide 1243.8225, Document Routing and Copy Distribution for Bioresearch Monitoring in ONADE

ATTACHMENT
Signature Page For The Freedom Of Information Summary

NADA OR ANADA #: _____
SPONSOR: _____
NAME OF DRUG: _____

CONCURRENCES: (Signature-date)		**CONCURRENCES WITH REVISIONS, IF REVISED**
1. _____ Primary Division Reviewer HFV-*xxx*	Date	_____ INITIAL
2. _____ Team Leader HFV-*xxx*	Date	_____ INITIAL
3. _____ Division Director HFV-*xxx*	Date	_____ INITIAL
4. _____ Division Director HFV-150 (if necessary)	Date	_____ INITIAL
5. _____ Quality Assurance Team, HFV-102	Date	_____ INITIAL
6. _____ Director, ONADE, HFV-100	Date	_____ INITIAL
7. _____ Director, CVM, HFV-1	Date	_____ INITIAL

Team/Reviewer: Attach this form to draft FOI Summary in Folder A of Approval Package.

HFV-199: Attach this form to FOI Summary when filed in NADA or ANADA.